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THE EFFECTS OF INANITION UPON THE STOMACH AND INTESTINES OF ALBINO RATS UNDERFED FROM BIRTH FOR VARIOUS PERIODS

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EFFECTS OF INANITION ON THE STOMACH AND INTESTINES OF ALBINO RATS UNDERFED FROM BIRTH FOR VARIOUS PERIODS *

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MINNEAPOLIS

Numerous observations have been made (chiefly by Jackson and Stewart) on the weight changes in the gastro-intestinal tract during periods of underfeeding in the albino rat, and similar studies have been made on other animals. The histologic changes during inanition have been less carefully studied, especially during the period of infancy. A thorough investigation of this problem seemed desirable, not only because of its general interest as a type of mammalian inanition, but also because of its special importance to human gastro-intestinal disorders. A brief summary of the results of this investigation was included in a report by Jackson.[1]

MATERIAL AND METHODS

One hundred and ten albino rats were used in the study. They are listed in two series. The first series comprised seventy-six rats. Fifty-three of these were test animals subjected to inanition by underfeeding from birth for various periods. Twenty-three were full fed controls. Thirteen of these controls were from the same litters as the test rats and were allowed to live until the last animal of the corresponding litter was killed. Such animals are designated as litter controls. Ten controls were taken from the stock cages of the colony. These are designated as weight controls, as they were of approximately the same body weight as the test rats at death.

The fifty-three test animals of the first series were chosen within twenty-four hours after birth, and were separated from the mother. They were returned to her at least once a day and allowed to nurse for a short time. The control animals from the same litter were allowed to remain continuously with the mother. The mother rats were fed with a standard normal diet used for the rat colony. In order to maintain a uniform degree of inanition the test animals were kept as nearly as possible at maintenance (constant body weight) for the maximum length of time. Some of the animals were able to secure more food than others and gained in weight. Such animals lived longer than those

* From the Institute of Anatomy, University of Minnesota.

1. Jackson, C. M.: The Effects of Inanition and Malnutrition Upon Growth and Structure, Philadelphia, P. Blakiston's Son & Co., 1925.

which were held slightly above or below the initial weight. In agreement with Aron,[2] Jackson [3] and Stewart,[4] it was found impossible to keep young rats alive for any extensive period, unless a slight increase in body weight was permitted. The test animals were killed in the last stages of starvation, or necropsy was performed immediately after death; but in no case were the animals used if rigor mortis was present, in order that postmortem changes might be avoided. The necropsy technic was similar to that employed by Jackson and Stewart. The weights of the liver, the spleen and in most cases the pancreas were also taken, as well as those of the alimentary canal. The stomach and intestines were weighed separately. Care was taken to prevent evaporation before and during weighing.

Regaud's neutral formalin Zenker fixing solution was used. The tissues were chromated according to Regaud's method. This permitted staining by the ordinary stains as well as by special stains. After fixation the tissues were embedded in paraffin and cut in sections two or three microns thick. Sections from each specimen were stained in one of the following: Delafield's hematoxylin and eosin; Unna's methylene blue and eosin; Altmann's aniline-water acid fuchsin, and counterstained with Mallory's connective tissue stain or with polychrome methylene blue; neutral gentian prepared according to Bensley.

The second series of rats comprised material used in a former study (Miller [5]) on the effects of inanition on the mitochondria. It included thirty-four albino rats older and larger than those used in the first series. Seventeen of these animals were allowed water only and were killed when in the last stages of inanition. The remaining seventeen were controls of the same age and of approximately the same body weight as the test rats. In this series no weights of the alimentary tract were taken.

The fixing solutions for this series were Bensley's osmic bichromate acetic and Regaud's neutral formalin Zenker. The staining was with Altmann's aniline-water acid fuschin stain, as modified by Bensley, and with Mallory's connective tissue stain.

An ordinary ocular micrometer was used in measuring the thickness of the coats of the stomach and the intestines. The measurements recorded are the averages from ten readings in each case unless other-

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2. Aron, H.: Nutrition and Growth, Philippine J. Sc., series B, **6**:1-51, 1911.

3. Jackson, C. M.: Changes in the Relative Weights of the Various Parts, Systems and Organs of Young Albino Rats Held at Constant Body Weight by Underfeeding for Various Periods, J. Exper. Zool. **19**:99-156, 1915.

4. Stewart, C. A.: Changes in the Relative Weights of Parts, Systems and Organs of the Young Albino Rats Underfed for Various Periods, J. Exper. Zool **25**:301-353, 1918.

5. Miller, S. P.: Effects of Various Types of Inanition Upon the Mitochondria in the Gastro-Intestinal Epithelium and in the Pancreas of the Albino Rat, Anat. Record **23**:205-210, 1922.

wise stated. The measurements of the cell diameters were made with a Leitz filar micrometer. A Zeiss 2 mm. apochromatic oil immersion lens with a compensating ocular was used. The measurements recorded are the averages from fifty readings in each case.

GROSS APPEARANCE AND WEIGHT CHANGES

Gross Appearance of the Body.—The bodies of the underfed rats are reduced in size when compared with the normal controls of the same litter. The hair in young rats is delayed in its appearance. It is shorter and rougher than that of the normal controls. The opening of the eyes is also delayed. The ears are white instead of normal pink. The skin appears tightly stretched over the feet and the tail, so that the bones are easily distinguished. This gives the tail a beaded appearance.

Gross Appearance of the Stomach.—In most cases the stomachs of the test rats contain food, even at death from inanition. At necropsy many stomachs are bloated with gas so that the walls of the cardiac portion appear transparent. Such stomachs may have a plug of undigested and curdled milk firmly packed in the pyloric opening. Other stomachs are quite flaccid, with only a small amount of bloody mucus in the pyloric region. The larger blood vessels appear congested as seen through the serosa.

The tunica mucosa of the cardiac region in the test rats appears normal and is glistening white. In the pyloric region this coat presents an abnormal, anemic appearance. By the use of a hand lens one may see numerous small ecchymoses distributed over the surface of the pyloric region. In many cases there are small ulcerated regions from 1 to 2 mm. in diameter.

Changes in the Weights of the Stomach.—For the study of the weight changes in the stomach, the data were secured from two sources. The weights of the stomachs of the controls and the test rats were observed directly. Weights of normal stomachs of the same body weight as each test rat were taken from the tables by Hatai.[6] As a check, the stomach weights of the controls were compared with the similar weights from Hatai's tables. There was only a small amount of variation, probably because of differences in the technic of weighing (fig. 1). The stomach weights from Hatai's tables were then used as a standard of comparison with those of the test rats of similar body weight. Two comparisons were made. The stomach weights of the normal rats from the tables and controls were made into a graph. To this graph were

6. Hatai, S.: On the Weight of the Epididymis, Pancreas, Stomach and of the Submaxillary Glands of the Albino Rat (Mus Norvegicus Albinus) According to Body Weight, Am. J. Anat. **24**:71-91, 1918.

added the individual stomach weights of the test rats (fig. 1). The stomach weights of the test rats were grouped according to body weight at death. The averages for these groups also were taken and compared with averages of similar groups of normal rats of the same average body weight.

In seven groups of test rats having an average body weight varying from 4.60 to 8.15 Gm., there were increases in the average weights of the empty stomachs from 51 to 149 per cent above the averages for normal rats of the same body weight. The test rats having an average body weight of 10 Gm. showed an increase of 133 per cent over the

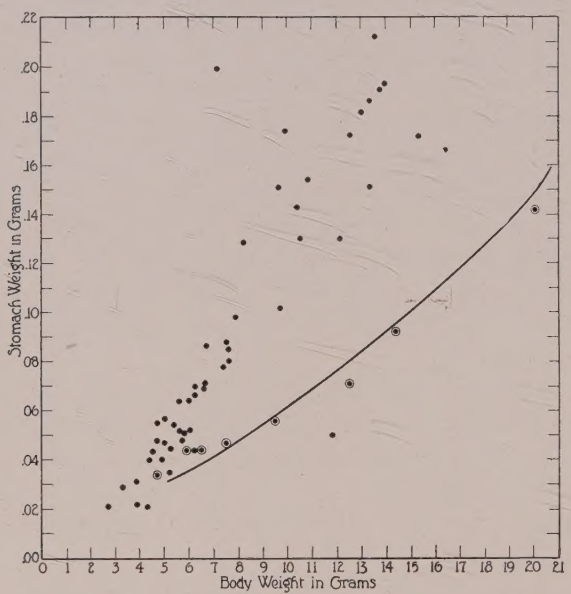

Fig. 1.—The relative weights of the stomach from the normal and the test rats; the normal curve is derived from the tables by Hatai; dots enclosed by circles are observed normal weights; solid dots are weights from test rats.

average weights of empty stomachs in normal rats of similar body weight. There was a similar increase of 102 per cent in the average empty stomach weight for the test rats having an average body weight of 13.9 Gm.

Gross Appearance of the Intestine.—The duodenum in the rats was often markedly congested, so that the wall appeared deep pink or even red. Usually it was partially filled with undigested milk, and occasionally it contains gas. The remainder of the small intestine in the test rats was deep orange or reddish brown. The color varied with amount of hemorrhage into the lumen of the intestine. In no case was the small intestine found entirely empty, even at death from starvation. In

approximately one half of the test rats the small intestine was dilated with gas. Often the distention was so great that the wall was thin and transparent.

The large intestine was usually pale pink. It was never completely empty and was often distended with gas. This was particularly noticeable in the case of the cecum. The blood vessels of the intestinal wall and of the mesentery often appeared congested.

Changes in the Weight of the Intestine.—The weights of the empty intestine of the test rats were taken without the mesentery and pancreas. The data for the normal weights of the stomach and the whole intestine were secured from Donaldson's tables.[7] The weights for the empty stomachs in the tables by Hatai [6] were subtracted from the total weights by Donaldson.[7] These data gave a series of weights for the normal

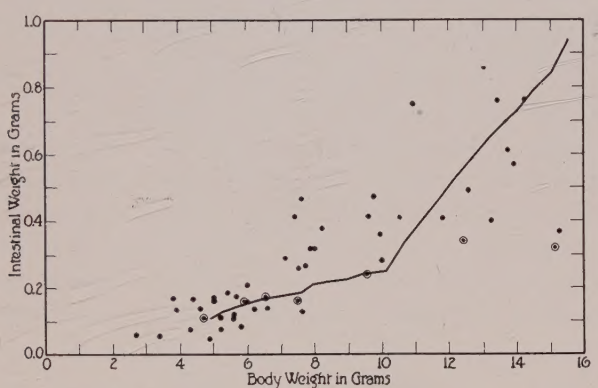

Fig. 2.—The relative weights of the intestine from the normal and the test rats; the normal curve is derived from tables by Donaldson and includes the weight of the pancreas and mesentery; dots with circle are observed weights of the normal intestine only; solid dots are observed weights of the intestine only from the test rats.

intestine including the pancreas and mesentery. My data do not include the weights of the latter structures, so it is possible to make only a relative comparison between the weights for the test rats and the normal data. The method of comparison is the same as that used for the stomach. The graph (fig. 2) gives the individual weights for the normal controls, and the normal curve derived from the tables by Donaldson and Hatai, with the individual weights of the intestines from the underfed test rats. The weights of the empty intestine were also arranged in groups according to body weight, and the averages of these were compared with similar averages for normal rats of the same

7. Donaldson, H. H.: The Rat, Memoirs of the Wistar Institute of Anatomy and Biology, ed. 2, no. 6, Philadelphia, Wistar Institute, 1924.

average body weights. In the groups with body weights of 4.60 and 5.38 Gm., the average weights for the intestine were 52 and 63 per cent above the averages of groups of normal rats of similar body weight. These results are in fair agreement with Stewart.[8]

The changes in the gastric and intestinal mucosa in my test rats resemble the descriptions by McCarrison [9] for adult pigeons and monkeys on diets deficient in various respects (vitamines, protein, salts, etc.). The small intestine of the rat was often greatly distended, but did not present the balloon-like expansions described by McCarrison for monkeys. The upper part of the colon was greatly distended in the test rats, as likewise found by McCarrison in monkeys. The pale color of the gastric mucosa and the frequent ecchymoses throughout the mucosa of the whole alimentary tract were observed by McCarrison. Similar atrophic changes in malnourished infants have been recorded by Baginsky,[10] Bloch,[11] Fischel [12] and others. The literature is fully reviewed by Jackson.[1]

The effects of inanition on the weights of the alimentary tract in rats have also been observed in a series of studies by Jackson and Stewart. Only a general comparison of their results is possible on account of different conditions involved. These differences include the age at which the animal was placed on the test, the character of the food and the severity of the inanition. Their data refer to the combined weight of the stomach and the intestine including the pancreas and mesentery, while mine are for the stomach and the intestine alone and separately.

HISTOLOGIC CHANGES

The changes in the histologic structure of the alimentary tract in the test rats include the structural changes of a regressive and atrophic nature and the changes in thickness of the various coats.

THE STOMACH

Tunica Mucosa.—The stomach in the rat is divided into two distinct parts. The cardiac or upper portion is lined with stratified squamous

8. Stewart, C. A.: Changes in the Weights of the Various Parts, Systems and Organs of the Young Albino Rats Kept at Birth Weight by Underfeeding for Various Periods, Am. J. Physiol. **48**:67-78, 1919.

9. McCarrison, R.: Studies in Deficiency Disease, Oxford Med. Publ., London, 1921.

10. Baginsky, A.: Die Verdauungskrankheiten der Kinder, Tubingen, 1884.

11. Bloch, C. E.: Untersuchungen über die Pädatrophie, Jahrb. f. Kinderh. **63**:421-445, 1906.

12. Fischel, R.: Diseases of Nutrition, in Pfaundler and Schlossman: Diseases of Children, Philadelphia, J. B. Lippincott Company, 1908, vol. 2, pp. 86-91.

epithelium. The pyloric or lower part contains the gastric glands and is covered with simple columnar epithelium. The stratified squamous epithelium forms a distinct fold or ridge separating the cardiac from the pyloric region. These divisions of the stomach and types of epithelial lining for the rat and allied species were described in the last century. A complete review of the literature is given by Oppel [13] in his comprehensive work on comparative histology.

The histologic changes in the cardiac portion during inanition are found chiefly in the stratified squamous epithelium. The intercellular spaces are more distinct than in normal tissue. These spaces are especially large in the stratum germinativum, in which they may be half the

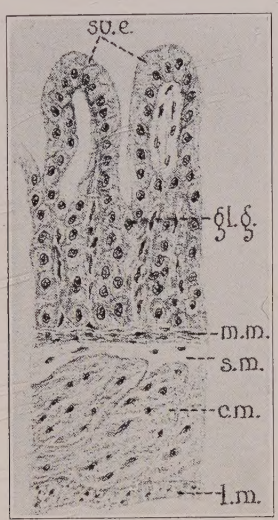

Fig. 3.—Section through the pyloric region of the stomach from a normal rat showing normal structure; body weight, 9.5 Gm.; age, 11 days. Magnification, 80 diameters; reduced one fourth; stain, hematoxylin and eosin. In this and figures 8 and 9: *c.m.* indicates lamina circularis; *gl.g.*, glandula gastrica; *l.m.*, lamina longitudinalis; *m.m.*, muscularis mucosae; *su.e.*, surface epithelium; *m.p.*, membrana propria; *s.m.*, submucosa.

width of the cell nuclei. The cytoplasm of these cells stains apparently normally, and there are no marked nuclear changes.

The normal gastric mucosa in the pyloric region of the albino rat resembles the descriptions of the same region in the mouse and other species of the rat, as reviewed in the work by Oppel. The normal surface epithelial cells have distinct boundaries and the cytoplasm is finely granular. Large mucous vacuoles lie near the free surface. The

13. Oppel, A.: Lehrbuch der vergleichenden mikroskopischen Anatomie der Wirbeltiere, Jena, Gustav Fischer, 1896, vol. 1-2.

chromatin is granular and uniformly distributed throughout the nucleus. The nuclear wall is distinct (fig. 3).

The surface epithelial cells in the test rats show various degrees of injury. In the rats underfed for the shorter periods the larger number of cells appear normal. Among these are cells with poorly defined borders. The cytoplasm stains faintly, the nuclear walls appear

Fig. 4.—Section through the base of the gastric glands from a test rat; body weight, 7.6 Gm.; age, 34 days; cells shrunken; almost total absence of secretory granules—those present reduced in size; nuclei irregularly shrunken. Magnification, 870 diameters; reduced one fourth; stain, neutral gentian. In this and figures 5, 6 and 7: *c.c.* indicates chief cell; *c.a.*, canalicular apparatus; *mtr.*, mitochondria; *n.*, nucleus; *p.c.*, parietal cell; *s.g.*, secretory granules.

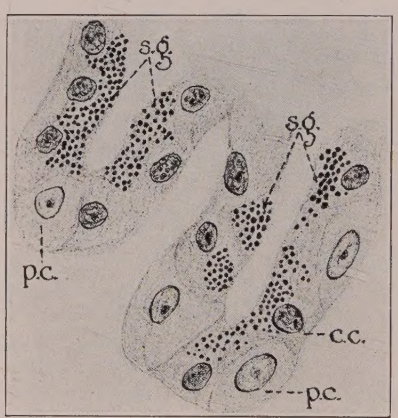

Fig. 5.—Section through the base of the gastric glands from the stomach of a normal rat; body weight, 9.2 Gm.; age, 43 days; chief cells show large numbers of secretory granules (*s.g.*); parietal cells apparently have no granules. Stain and magnification same as in figure 4.

irregular and the mucous vacuoles are reduced in size or may be absent altogether. Other cells show a coarsely reticulated cytoplasm, containing large nonmucous vacuoles. The nuclei are pyknotic or in various stages of karyorrhexis or karyolysis.

In the rats underfed for the longer periods there is an increased number of the injured cells, especially those showing the more pro-

nounced atrophic changes. However, there are always some cells which appear nearly normal. The cells lining the foveolae gastricae show similar injuries in varying degrees.

The gastric glands appear shrunken into the test rats. The amount of apparent shrinkage is greater in the rats underfed for the longer periods. The chief cells of the gastric glands appear somewhat smaller than those from the normal glands. Their cytoplasm stains poorly; the nuclei are pyknotic and stain faintly. In many cells the nuclei show stages of karyorrhexis or karyolysis. Specimens stained with neutral gentian show a reduced number and even an absence of secretory granules (fig. 4). Specimens from normal rats have these granules in large numbers (fig. 5). Paneth cells show a similar reduction of granules. The normal acid cells stained with acid fuchsin contain a large number of intensely staining cytoplasmic granules. These granules appear in groups with irregular branching spaces between them. Such

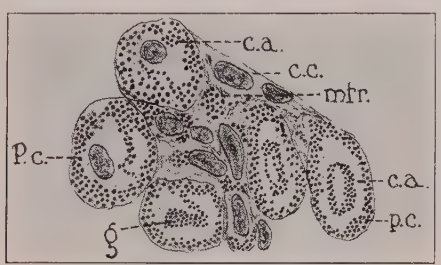

Fig. 6.—Section near the base of the gastric glands from the same normal rat as was used in fig. 5; showing granules in acid cells and canalicular apparatus. Stain, acid fuchsin and Mallory's connective tissue stain; magnification same as in fig. 5.

spaces are evidences of the canalicular apparatus (fig. 6). In the test rats the acid cells appear shrunken (fig. 7), and the canalicular apparatus is not visible. The granules appear to be reduced in number but they retain their brilliant staining reaction. Measurements of the acid cells show a decrease of from 19 to 37 per cent for the average lesser cell diameter in rats underfed for from fourteen to thirty-four days. The greater diameter is more variable.

In the areas of the gastric mucosa in which there were ecchymoses, the changes in the histologic structure are extreme. The surface cells are in most cases necrotic and form sheetlike masses of faintly staining disintegrating cells. These appear somewhat like a membrane on the surface of the mucosa (fig. 8). The gastric glands appear as strands of disintegrating and necrotic cells. The cell boundaries are difficult to determine and the nuclei show advanced stages of degeneration (fig. 8). The lamina propria in most of the test rats shows evidence of edema.

The edema is more pronounced in the rats underfed for the longer periods. The connective tissue cells appear somewhat shrunken. There is apparently no cell infiltration.

Tela Submucosa.—Structural changes in the tela submucosa are not well defined. In some instances there is apparently a slight edema. The blood vessels appear congested, but similar appearances are often observed in the normal rats. Occasionally the test rats show small hemorrhages in the submucosal spaces. Typical inflammatory conditions do not appear.

Tunica Muscularis.—The muscle cells show atrophic changes more frequently in the lamina circularis. Some of the muscle cells undergo a degeneration. The cytoplasm is at first granular, later it becomes clear and hyaline in appearance, while later it may be filled with connective tissue.

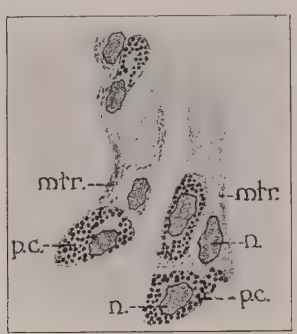

Fig. 7.—Section through the base of the gastric gland from the same test rat as was used in fig. 4; showing shrunken cells and the absence of canalicular apparatus; granules in parietal cells remain brilliantly stained. Stain and magnification as in fig. 4.

Changes in Thickness.—In spite of the regressive and atrophic changes in the tunica mucosa of the test rats, this layer continues to grow in thickness (figs. 3 and 9). The stratified squamous epithelium of the cardiac region is increased 53 per cent in thickness in a group of test rats having an average body weight of 9.66 Gm. (comparisons being with normal rats of similar body weight). The epithelial ridge separating the cardiac from the pyloric region in the same groups likewise shows an increase of 69 per cent in thickness. There is also a continued growth in the height of the gastric glands in the test rats. In some of the test animals the height of the glands is twice that in normal rats of the same body weight. In a group of test rats with an average body weight of 7.78 Gm. the average height of the gastric glands is 71 per cent greater than the normal.

Measurements of the submucosa in both the normal and the test rats are too variable to draw conclusions. Measurements of the tunica

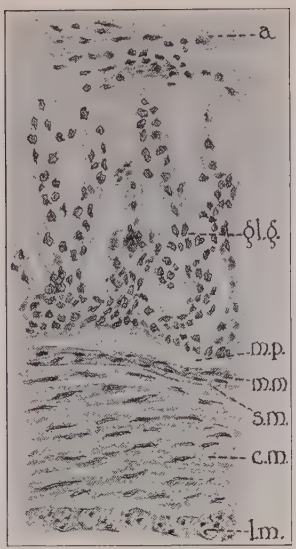

Fig. 8.—Section through the atrophic area from the pyloric region of the stomach from a test rat; body weight, 7.6 Gm.; showing atrophic tunica mucosa: *a* indicates necrotic epithelium; *m.p.*, edema in membrana propria; degenerating nuclei of the gastric gland may be seen. Magnification, 80 diameters; reduced one fourth.

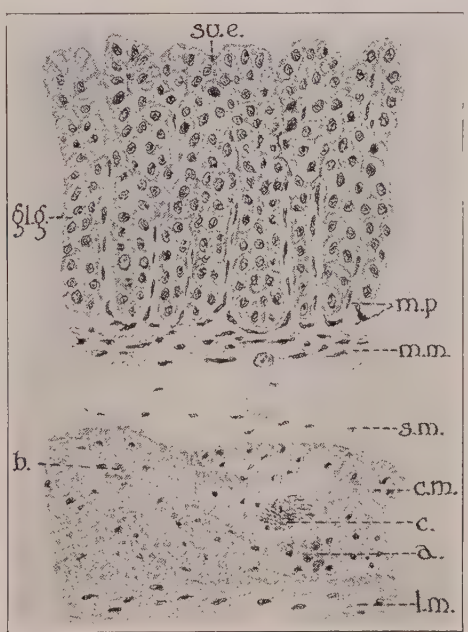

Fig. 9.—Section through the pyloric region of the stomach from a test rat; body weight, 9.66 Gm.; showing shrunken nuclei in the surface epithelium and gastric glands; slight edema in the membrana propria at the base of the gastric glands; and an area of degeneration in the tunica muscularis: *a* indicates swollen cells; *b*, irregular shrunken cells; *c*, complete degeneration. Magnification, 80 diameters; reduced one fourth; stain, hematoxylin and eosin.

muscularis show a decrease of 30 per cent in the thickness of the lamina circularis in the test rats. The thickness of the lamina longitudinalis was so variable for both the normal and the test rats that conclusions are not justified.

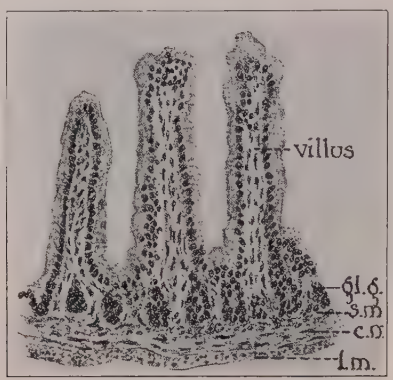

Fig. 10.—Section through the duodenum from a normal rat; body weight, 6.5 Gm.; age, 2 days; showing normal villi, glands of Lieberkühn and the various tunics. Stain, hematoxylin and eosin; magnification, 80 diameters; reduced one fourth. In this and the following figures: *c.m.*, indicates lamina circularis; *gl.l.*, gland of Lieberkühn; *m.p.*, membrane propria; *l.m.*, lamina longitudinalis; *s.m.*, tela submucosa; *su.e.*, surface epithelium.

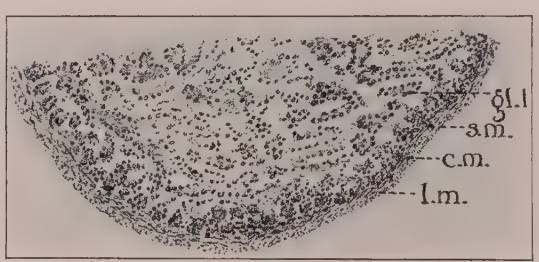

Fig. 11.—Section through the duodenum from a test rat; body weight, 7.6 Gm.; age, 34 days; showing degenerated epithelium and villi in the lumen, shrunken glands of Lieberkühn, and other tunics with retarded growth; comparison should be made with fig. 10. Stain, hematoxylin and eosin; magnification, 80 diameters; reduced one fourth.

SMALL INTESTINE

Tunica Mucosa.—The epithelial cells of the small intestine exhibit similar changes of varying intensity. In many of the test rats the villi are in part or totally disintegrated. The lumen of the intestine is often filled with masses of degenerated cells (comparison should be

made with figs. 10 and 11). The glands of Lieberkühn appear shrunken, with atrophic cells. The cytoplasm stains poorly. The cell boundaries are difficult to determine. The nuclei show pyknosis and stages of karyorrhexis or karyolysis. When stained with neutral gentian, the Paneth cells in these glands show the granules decreased or absent. There appears to be a small amount of edema in the lamina propria, but no cell infiltration.

Tunica Submucosa.—This layer does not show well defined edema. There are no evidences of inflammation.

Tunica Muscularis.—Atrophy of the muscle cells is not as well defined as in the stomach.

LARGE INTESTINE

Tunica Mucosa.—In the test rats, changes are less evident in the tunica mucosa of the large intestine than in that of the small intestine

Fig. 12.—Section of the large intestine from a normal rat; body weight, 12.5 Gm.; age, 10 days; showing normal structure. Stain, hematoxylin and eosin; magnification, 80 diameters; reduced one fourth.

or the stomach. The surface epithelium shows but slight changes in its faintly staining cytoplasm. The cell boundaries are somewhat less clearly defined than in the normal, and the nuclei present slightly irregular walls. The glands appear somewhat shrunken. Their cells show various degrees of injury. There is a variable amount of edema in the lamina propria (comparison should be made with figs. 12 and 13).

Tunica Submucosa.—The edema is usually slight in this tunic as in case of the stomach and the small intestine of the test rats. Occasionally there are hemorrhages of the small submucosal vessels apparently.

Tunica Muscularis.—This coat likewise showed but little change in the test rats. No atrophy of the muscle cells was observed.

Changes in the Thickness.—Changes in the thickness of the coats of both the small and the large intestine are apparently also less than in the

stomach. Measurements of the tunica mucosa of the small intestine were unsatisfactory because of the degeneration of the villi. Those for the tunica submucosa were variable and inconclusive. The lamina circularis of the tunica muscularis is somewhat reduced in thickness in the test rats. The lamina longitudinalis apparently does not decrease in thickness. No measurements were made for the large intestine. However, there is an increased growth of the tunica mucosa, similar to that in the stomach.

Histologic changes somewhat similar to those described for the test rats are recorded by McCarrison [9] for adult pigeons, guinea-pigs and monkeys dying from various deficiencies in the diet. In many cases the

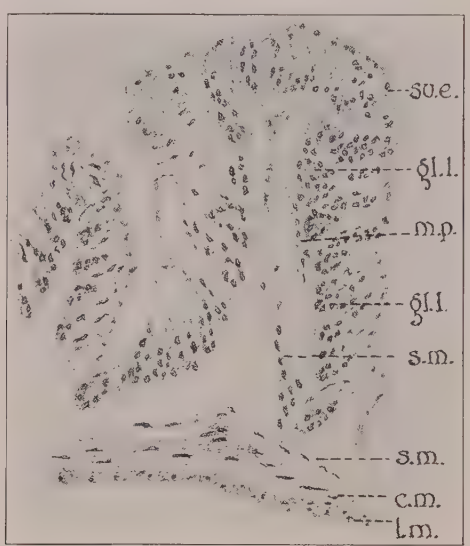

Fig. 13.—Section of the large intestine from a test rat; body weight, 13 Gm.; age, 43 days; showing continued growth of the mucosa, edema in membrane propria, shrunken glands of Lieberkühn and abnormal nuclei; comparison should be made with fig. 12. Stain, hematoxylin and eosin; magnification, 80 diameters; reduced one fourth.

epithelium was largely necrotic, as in the extreme atrophic regions of the gastric mucosa in my test rats. Capillary hemorrhages in the gastric mucosa were frequently noted by McCarrison. Gastric hemorrhages (ecchymoses) were likewise found in my test rats, and also occurred in the small intestine. McCarrison describes edema in the lamina propria, which likewise occurred in my test animals. However, I did not observe the edema which he describes in the tunica muscularis in the vicinity of Auerbach's or Meissner's plexuses. The atrophy of the gastric tunica muscularis was apparently greater in McCarrison's animals than in mine.

Parrot,[14] Fischel,[12] Schelble[15] and Aschoff[16] give descriptions of variable changes in the gastric tunics in malnourished human infants.

The changes from the normal in the structure of the small and the large intestine in my test rats are also similar in many respects to those described for other types of inanition. Shrinkage and degeneration of the villi in starved puppies was described by Quattrochi.[17] The descriptions by McCarrison for test animals fed on various inadequate diets correspond in general to those given for my test rats. The literature on this topic is comprehensively reviewed by Jackson.[1]

SUMMARY

1. In albino rats severely underfed from birth for various periods of time (to forty-three days), the weights of the empty stomach and intestine were much greater than in normal (younger) rats of similar body weight. The increase in the weight of the stomach appeared relatively much greater than that of the intestine.

2. In comparison with younger controls of similar body weight, there also appeared in the test rats a marked absolute increase in the thickness of the gastric tunica mucosa. This in part accounted for the increase in gastric weight. There was, however, a decrease in the thickness of the tunica muscularis.

3. Histologic preparations also showed a variable amount of edema in the lamina propria of the gastric mucosa in the test rats. The edema was more severe in the rats underfed for the longer periods of time, and also might in part account for the increased gastric weight. Stomachs with the most marked edema showed the greatest apparent increase in weight.

4. In spite of the increased growth in the weight and thickness, the gastric mucosa in the test rats showed regressive structural changes to a variable extent. These changes included atrophy and degeneration in restricted areas of the surface epithelium. The cells showed nuclear degeneration and cytoplasmic changes, including vacuolization and loss of secretory granules. In extreme inanition the tunica mucosa became almost completely necrotic in some instances.

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15. Schelble, H.: Bakteriologische und pathologisch-anatomische Studien bei Ernährungsstörungen der Säuglinge, Leipzig, Georg Thieme, 1910.

16. Aschoff, Ludwig: Pathologische Anatomie, ed. 15, Leipzig, Johann Ambrosius Barth, 1921, vol. 1, p. 752-753.

17. Quattrochi, S.: Alterazione del tubo gastroenterico di cagnolini resi atrofici per insufficiente, cattira, o irregolare alimentazione, Pediatria **9**:49-67, 1901.

5. Distinct changes from the normal structure were not apparent in the gastric tela submucosa, except for occasional hemorrhages from the submucosal vessels.

6. The gastric tunica muscularis in the test rats showed a variable degree of atrophy and degeneration in the muscle cells. The degeneration did not involve the whole thickness of the tunica but occurred in restricted regions. In some places the muscle cells completely disappeared and were replaced by fibrous connective tissue.

7. In the small intestine of the test rats the villi appeared variably atrophic and in extreme cases were completely disintegrated.

8. The intestinal glands of Lieberkühn likewise appeared atrophic and decreased in size, with degenerative nuclear and cytoplasmic changes.

9. The lamina propria in the small intestine of the test rats showed edema which doubtless, as in the stomach, was a factor in causing the increase in weight.

10. The tunica muscularis of the small intestine in the test rats did not present such marked atrophy of the muscle cells as that which appeared in the stomach.

11. The large intestine in the test rats showed changes in general similar to those observed in the stomach. The tunica mucosa increased in thickness. Regressive changes of the surface epithelium and of the glands of Lieberkühn were observed. There was edema in the lamina propria and to a slight extent in the submucosa. Definite atrophy in the muscle cells in the tunica muscularis was not observed, however.

12. The histologic changes observed in the test rats during the present chronic underfeeding experiments resembled more or less those described by other investigators in the alimentary tract of various animals subjected to different types of total or partial inanition. They also somewhat resembled those described for atrophic infants, but appeared in general more pronounced, and less variable.

VITA

The author, Shirley Putnam Miller, was born June 17, 1878 in Rockwell, Iowa. He received the degree of B.S. in 1903 from South Dakota State College, and the degree of M.A. from the University of Minnesota in 1904. He was a student in the University of Berlin from 1909 to 1912, in the departments of anatomy and paleontology. In 1916-17 he was a research fellow in anatomy in the University of Minnesota.

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